

## REMARKS

The Office has restricted the present application as follows:

Group I – Claims 51, 59-63 and 70-71;

Group II – Claims 52-58;

Group III – Claims 64, 66, 68 and 69;

Group IV – Claims 65 and 67; and

Group V – Claim 72.

The Office has further restricted:

Group I to each type of therapeutic agent or combination thereof, and the specific source and enzyme, if applicable; and

Group II to each specific translocation domain.

**Applicants elect, with traverse, Group II, Claims 52-58, with a Domain Election Requirement election of the translocation domain from *C. botulinum*.**

The Office has characterized each specified Group as lacking the same or corresponding special technical feature. The Office has characterized the same or corresponding special technical feature of the Groups as a composition comprising a therapeutic agent which inhibits a Rho GTPase, and a neuronal cell targeting component comprising an Hc domain of botulinum C1 toxin. Finally, citing PCT Publication WO 00/28041 (Shone *et al.*) for describing superoxide dismutase linked to a neuronal cell targeting domain, and discussing botulinum C1 toxin as a targeting neurotoxin; and Heo *et al.*, for describing that superoxide dismutase as a therapeutic agent which inhibits a Rho GTPase, the Office asserts that the special technical feature of the Groups does not define a contribution over the art.

Applicants respectfully traverse the Office characterization of the special technical feature of the Groups: the special technical feature of the Groups is a composition comprising a therapeutic agent which inhibits a Rho GTPase, and a neuronal cell targeting component comprising an Hc domain of botulinum C1 toxin,

**wherein the Hc domain has been made recombinantly.** This distinction is very significant: Shone *et al.* discuss botulinum C1 toxin as a targeting neurotoxin, not the Hc domain of botulinum C1 toxin made recombinantly. Furthermore, as noted on page 3, lines 10-15, of the present application, the Hc domain of botulinum C1 toxin made recombinantly has significantly reduced affinity and specificity for neuronal cells, up to the point where there is no effective targeting of neuronal cells. Therefore, the Hc domain of botulinum C1 toxin made recombinantly is distinct from botulinum C1 toxin described by Shone *et al.*, since their affinity and specificity for neuronal cells is so different. Applicants submit that the claims do have the same or corresponding special technical feature. Withdrawal of the Restriction Requirement is respectfully requested.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Paul E. Rauch', is written over a horizontal line.

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